22.1 Mendelian Inheritance

Mendelian inheritance refers to the patterns of inheritance that are characteristics of organisms which reproduce sexually.

Gregor John Mendel was an Austrian monk who formulated some of the fundamental principles regarding the inheritance of traits. Between 1856 – 1865, he performed number of experiments in which he cross-bred pea plants (*Pisum sativun*) with 7 pairs of contrasting characteristics Mendel explained his results by describing two laws of inheritance that introduced the idea of dominant and recessive genes. (Fig.22.1)

Character			F_2 Generation Ratio
Dominant Form	x	Recessive Form	
Purple flowers	x	White flowers	(3/4:1/4)
Yellow seeds	x	Green seeds	(3/4:1/4)
Round seeds	x	Wrinkled seeds	(3/4:1/4)
Green pods	x	Yellow pods	(3/4:1/4)
Inflated pods	x	Constricted pods	(3/4:1/4)
Axial flowers	x	Terminal flowers	(3/4:1/4)
Tall plants	x	Dwarf plants	(3/4:1/4)

Fig.22.1 Mendel's Seven Contrasting Pairs of Characters

22.1.1 Association of Inheritance with Laws of Mendel

Gregor John Mendel, through his work on pea plants, discovered the fundamental laws of inheritance. He deduced that factors (genes) come in pairs and inherited as distinct units, one from each parent. Mendel tracked the segregation of parental genes and their appearance in the offspring as dominant and recessive traits. He recognized the mathematical patterns of inheritance from one generation to the next. On the basis of his series of experiments on pea plants he formulated following laws:

> **Extra Information**
>
> On genetic level all humans are more than 99% identical.

1. The Law of Segregation

The law of segregation states that the two alleles of a single trait will separate randomly. Each inherited trait is called factor (gene) pair. Parental factors (genes) are randomly separated to the sex cells so that sex cells contain only one member of the factor (gene) pair. Offspring, therefore, inherits one allele from each parent when sex cells unite in fertilization.

2. The Law of Independent Assortment

The law of independent assortment states that the allele of one gene separate independently of another allele. Genes for different traits are sorted separately from one another so that the inheritance of one trait is not dependent on the inheritance of another.

> **Extra Information**
>
> The term Mendalian inheritance refers to a set of rules that revolve around the passing down of hereditary traits from parents to offsprings.

Inheritance of Single Trait (Monohybrid Cross)

The Law of Segregation

Mendel carefully selected 7 pairs of contrasting characters for his experiments. First he experimented plants with one pair of contrasting characters such as tallness and shortness of the plants. This type of cross which involves only one pair of contrasting characters is called monohybrid cross.

Procedure and Observations

In one of his experiments, Mendel crossed tall pea plants (about 2 meters high) with dwarf pea plants (about 20 – 50 cm). He used pure breeding varieties *i.e.* plants which when self-fertilized produced offsprings that resembled their parents. He crossed pollinated tall plants with pollen from dwarf plants and vice versa. He planted the seeds from these plants and observed the resulting hybrid which he called the **first filial generation** or **F_1 generation.** In F_1 generation all plants were tall. He then allowed F_1 plant to self-pollinate and produced seeds which gave rise to **F_2 (second filial)**

generation. In F_2 he got 1064 plants. Out of these 1064 plant 787 were tall plants and 277 dwarf plants *i.e.* in the ratio of about three tall one dwarf (3:1).

Mendel also made crosses using 6 other contrasting characters of pea plants and got almost similar results.

In all his experiments, Mendel observed that one trait or character appeared in F_1 generation while other disappeared. However, this character reappeared in F_2 generation but only in about $1/4^{th}$ of the total number of offspring. The character which appeared in F_1 generation is called **dominant** while the character which could not express itself in F_1 generation is called **recessive** trait.

Interpretation of the Results

On the basis of these experimental results Mendel was able to suggest a mechanism to explain the observations, he had made about pea plants. Infact, he suggested a model of how the inheritance of traits could be explained. Mendel concluded that:

- Hereditary characters are responsible for transmission of characteristics.
- Each characteristics is controlled by a pair of factors (genes) in the cell of an organism *e.g.* colour of flower, colour of seed, shape of seed, height of plant, *etc.*, are controlled by a pair of factor.
- If the two factors differ then only the dominant one will show its effect *e.g.* if a pea plant contains one factor for tallness and one for dwarfness, only the tall (dominant) will show the effects.
- The two factors in each pair separate or segregate during gamete formation and each gamete will contain only one factor. This statement is known as Mendel's law of segregation.

Hence when a pea plant containing a factor for tallness and a factor for shortness produces gametes. A particular gamete will either have tall factor or the dwarf factor but not both. Thus the gametes are always pure.

- The fusion of haploid gametes at fertilization restores the diploid condition in the zygote.
- Gametes unite at random so that a predictable ratio of characteristics occur among the offsprings.

Dominant Gene

It is able to express itself even in the presence of its recessive allele and does not require similar allele to produce its effect.

Recessive Gene

It is unable to express its effect in the presence of dominant allele so it produces phonotypic effect only in presence of similar allele.

Extra Information

The term dominant and recessive do not mean that an organism possessing a dominant trait is healthier or more vigorous than an organism with the recessive trait. Both dominant and recessive alleles can be disease carrier.

Inheritance of Two Traits (Dihybrid Crosses)

Mendel's Law of Independent Assortment

Mendel suggested his second law of inheritance by following two characters at the same time, such as seed color and seed shape. Pea seeds shape may be either round (smooth) or wrinkled. From single character crosses, Mendel knew that allele for yellow seed is dominant (Y), while allele of green seed is recessive (y). He also knew that allele from round seed is dominant (R), and allele for wrinkled is recessive (r).

Procedure and Observations

Mendel crossed pure **round-yellow seeded plant (RRYY)** with **wrinkled green seeded plant (rryy)** and got F_1 generation. In F_1 generation, he got all round-yellow seeded plants. However, these plants will be dihybrids *i.e.* RrYy. The key step in the experiment is to see what happens when F_1 plants self-pollinate and produce F_2 generation. If the hybrids transmit their allele in the same combinations in which the alleles were inherited from parental generation, then the F_1 hybrid will produce only two classes of gametes: RY and ry. This dependent assortment hypothesis predicts that the phenotype ratio of F_2 generation will be 3:1, just as in monohybrid cross.

Interesting Information

Pure bred means that if you let the plant self-fertilize, the offsprings will always look exactly like their parents *i.e.* if the tall plants were crossed then the offspring will always be tall.

The alternative hypothesis is that the two pairs of allele segregate independently of each other. In this example the F_1 plant will produce 4 types of gametes in equal quantities *i.e.* RY, rY, Ry, ry. If sperm of the 4 classes fertilize eggs of the 4 classes, there will be 16(4×4) equally probable ways in which the alleles can combine in F_2 generation. These combinations result in 4 phenotype categories with a ratio of 9:3:3:1. Nine will be round-yellow, three will be wrinkled yellow, three will be round-green and one will be wrinkled green. When Mendel did the experiment and obtained F_2 generation, his results were close to the predicted 9:3:3:1 phenotypic ratio. These results were supporting the hypothesis that the allele for one gene-supporting seed colour and seed shape are sorted into gametes independently of the alleles of other genes.

Interpretation of the Results

Mendel tested all seven pairs of contrasting characters in various dihybrid combinations and always observed a 9:3:3:1 phenotypic ratio in F_2 generation. Is this consistent with the 3:1 phenotypic ratio observed for the monohybrid crosses? To investigate this question, let's consider one of the two dihybrid characters by itself. Looking only in pea color we see that there are 416 yellow and 140 green peas, a 2.97:1 ratio, or roughly 3:1 ratio. In this dihybrid cross, the pea color alleles segregate as this were a monohybrid cross. The result of Mendel's dihybrid cross is the basis for what is

called **law of independent assortment**. This law states that the alleles of two (or more) different genes get sorted into gametes independently of one another. In other words, the allele a gamete received for one gene does not influence the allele received from another gene.

Limitations of the Law of Independent Assortment

This law applies only to those genes (allele pairs) located on different chromosomes (non-homologous chromosomes) or alternatively to genes that are very far apart on the same chromosome. All the pea characters Mendel chose for analysis were controlled by genes on different chromosome. This situation greatly simplified interpretation of his multi-character pea crosses.

Usefulness of Law of Independent Assortment

This law explains that desired characters of two parents can be expressed in single parents and undesired characters can be prevented from expression. Can you guess how?

Scope of Independent Assortment in Variation

The independent assortment genes also contribute in mutation because it results in the shuffling of chromosomes into various gametes. Crossing over occurs when homologous chromosomes exchange genetic information. Thus, chromosomes are formed that contain genes from both parents. (Fig.22.2)

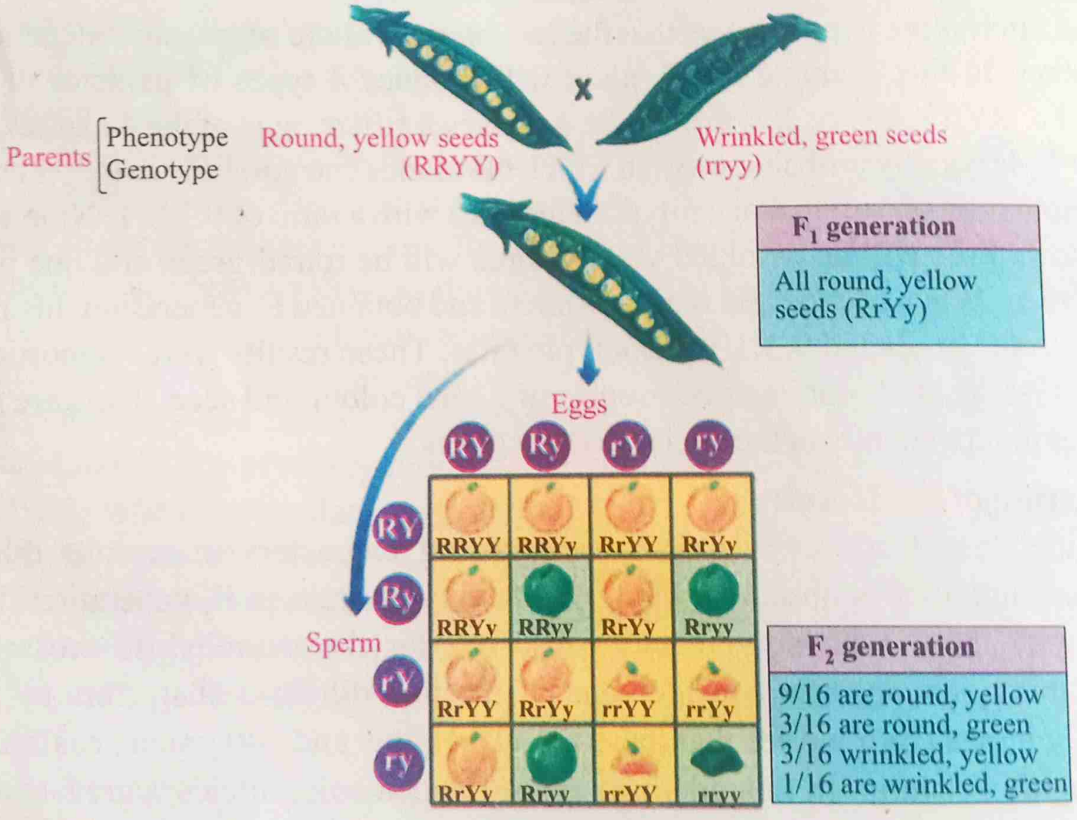


Fig.22.2 Dihybrid Cross

22.1.2 Inheritance and Mathematical Probabilities

Probability is a chance of occurring of an event. Mendel laws reflect the same rules of probability that apply to tossing coins, rolling dice and drawing cards from a deck. The probability scale range from 0 to 1. An event that is certain to occur has a probability of 1, while an event that is certain not to occur has a probability of 0 with a normal coin, the chance of tossing tails is 1/2 and chance of tossing heads is 1/2.

Tossing a coin illustrates an important lesson about probability. For every toss, the probability of head is 1/2. The out-come of any particular toss is unaffected by what has happened on previous trials.

The phenomena such as coin tosses are referred as independent events. Each toss of a coin whether done sequentially with one coin or simultaneously with many is independent of every other toss. And like two separate coin tosses, the alleles of the one gene segregate into gamete independently of another gene's alleles (the law of independent assortment). The combined probability of two or more independent events can be calculated by product rule.

Product Rule

This rule states that probability of two or more independent event occurring together can be calculated by multiplying the individual probability. This rule is useful in genetics. The product rule is used to predict frequencies of fertilization events.

According to this rule the probability of round yellow phenotype in F_2 generation of a dihybrid cross is equal to the product of individual probabilities of round (3/4) and yellow (3/4) phenotype *i.e.* $P=3/4\times3/4=9/16$.

22.2 Exceptions to Mendelian Inheritance

We know today that there are many exceptions to Mendel's laws. It means that not every gene has alleles that are strictly dominant or recessive. Does this mean that Mendel was wrong? No it means that we know more today about genetics, diseases and inheritance than 150 years ago, when Mendel formulated his laws. Some of the most common exceptions of Mendelian inheritance will be discussed here.

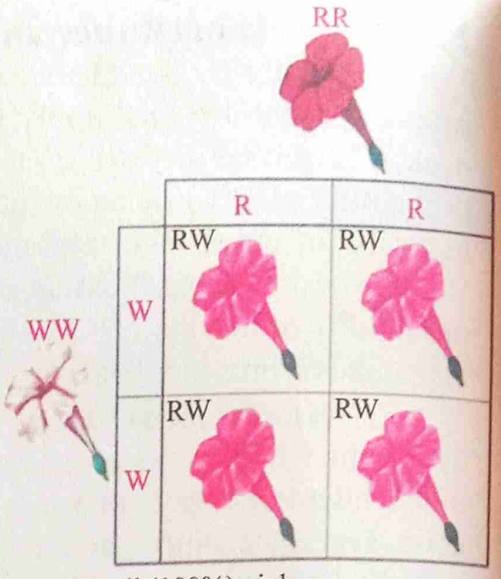
22.2.1 Incomplete Dominance

When two contrasting characters are crossed, and if in F_1 generation none of the characters is fully expressed then this phenomenon is called incomplete dominance. It was first described by Carl Correns.

Example: When red (RR) Japanese 4 o'clock flower plant (*Mirabilus Jalapa*) is crossed with white (WW) 4 o'clock flower plant, in F_1 generation hybrid plant have pink (RW) flowers. This third intermediate phenotype results from the flowers of heterozygotes having less red colour than the red homozygotes. This is unlike the case of Mendel's pea plant. (Fig.22.3)

At first glance incomplete dominance of either allele seems to provide evidence for the blending hypothesis of inheritance which would predict that red or white traits

could never reappear among offsprings from pink hybrid. In fact, inbreeding F_1 hybrids produce F_2 offsprings with a phenotypic ratio of one red to two pink to one white *i.e.* 1:2:1 ratio. Thus genotype and phenotype ratio is same (RR, 2RW, WW). The segregation of the red flower and white flower alleles in the gametes produced by the pink flowered plants confirms that the allele for flower colour are heritable factors that maintain their identity in the hybrids; that is; inheritance is particulate.



F_1 all (100%) pink

F_2 one red (25%), two pink (50%), one white (25%)

Fig. 22.3: Incomplete Dominance

22.2.2 Co-dominance

The dominance relation when two contrasting characters are crossed and in F_1 generation both of them fully express themselves is called co-dominance.

For example, the human MN blood group is determined by co-dominant alleles for two specific molecules located on the surface of red blood cells, the M and N antigen molecules. A single gene locus at which two allelic variations are possible, determines the phenotype of this blood group. Individual homozygous for the M allele MM have red blood cells with only M molecules; individual homozygous for the N allele NN have RBCs with only N molecules. But both M and N molecules are present on the red blood cells of individuals heterozygous for the M and N alleles (MN). The MN phenotype is not intermediate between the M and N phenotypes, which distinguishes co-dominance from incomplete dominance. Rather, both M and N phenotypes are by heterozygotes, since both molecules are present. (Table 22.1-22.2)

Genetic Problem

What would be expected offspring when red four O'clock plant is crossed with pink one.

Solution:

Red	X	Pink	
RR	X	RW	
RR	RW	RR	RW
Red	Pink	Red	Pink

Ratio = 2:2

Skill

What will be the result of cross between red bulls to white cow? What will be genotype and phenotype of offspring?

Table 22.1: MN Blood Group Showing Co-dominance

Genotype	Phenotype	Antigen Present on red BC
L^ML^M	M	M
L^ML^N	MN	M and N
L^NL^N	N	N

Table 22.2: Difference between Incomplete Dominance and Co-dominance

S. No.	Incomplete dominance	Co-dominance
i)	Intermediate trait appear.	Has independent effect. Both traits simultaneously appears.
ii)	Both alleles are expressed itself partially.	Both alleles are equally conspicuous.
iii)	None of the parental characteristics express in offspring.	Both parental characteristics express in offspring.

Multiple Allele

Any one of a series of three or more alternative or allelic forms of a gene, only two of which can exist in any normal diploid individual is known as multiple allele.

The ABO blood group is an example of multiple allele. It is also an example of exception to Mendelian inheritance.

The 4 blood groups A, B, AB and O are all determined by a single gene. Three alleles of this gene exist. I^A, I^B and i. I^A and I^B are dominant while i is recessive to both I^A and I^B.

22.3 Blood Group System

Although the ABO and Rh-groups are most important for blood transfusions, there are 36 other known blood group that usually do not complicate the blood transfusion are called **rare types**.

Each blood group has a combination of sugars and protein called antigens that are found on the surface of RBCs. There are about 600 antigens so there is potential for a lot of variation between different people.

22.3.1 ABO Blood Group System

ABO blood group is an example of multiple allele which is an exception to Mendelian inheritance. In 1900 **Karl Landsteiner** reported a series of test, which identified the ABO blood group system. He got noble prize in 1910 for his discovery. The ABO blood group is also found in other **primates** like apes, chimpanzees, gorillas.

Extra Information

There is no crossing over between the members of multiple allele. Crossing over takes place between two different genes only and does not occur within gene.

Antigen of ABO Blood Group

ABO antigens are glycolipid in nature, attached on the surface of red blood cells. These antigens stick out from cell membrane and there are many antigen sites per red blood cell. Besides their presence on red blood cells, soluble antigens can be present in plasma, saliva and other secretions. These antigens are also expressed on tissues other

than red blood cells. There are two types of antigens *i.e.* antigen A and B. The presence or absence of these antigens makes 4 types of blood groups *i.e.* blood group A when antigen A is present, blood group B when antigen B is present, blood group AB when both antigens A and B are present and blood group O when both antigens A and B are absent.

Genetic Basis of ABO System

Blood groups are inherited from both parents. The ABO blood group is controlled by a single gene with three types of alleles *i.e.* I^A, I^B and i. The I stands for isoagglutinogen. The I^A and I^B both are dominant alleles, while 'i' is recessive. The gene is located on long arm of chromosome no 9. The individual with genotype I^AI^A and I^Ai have type A blood group and individual with I^BI^B and I^Bi have type B blood group.

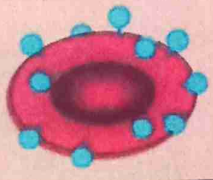
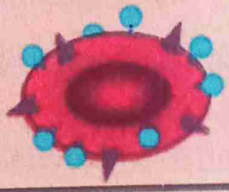
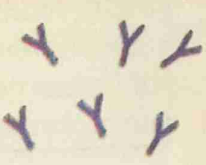
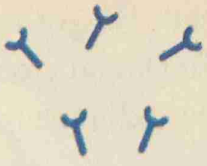
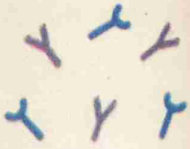
Problem

A man of blood group B and women of blood group A have three children. One is group A, one group B and one group O. What are the genotype of five people?

The genotype I^AI^B have blood group AB because both I^A and I^B alleles are dominant. An individual having genotype ii has blood group O.

Codominance: Another example of codominance is human blood type AB, in which two types of protein ("A" and "B" appear together on the surface of blood cells. (Table:22.3)

Table 22.3: ABO Blood Group Antibodies and Antigens

ABO Blood Groups				
Antigen (on RBC)	Antigen A 	Antigen B 	Antigen A + B 	Neither Antigen A nor B 
Antibody (in plasma)	Anti-B Antibody 	Anti-A Antibody 	Neither Antibody	Both Antibodies 
Blood Type	**Type A** Cannot have B or AB Blood Can have A or O Blood	**Type B** Cannot have A or AB Blood Can have B or O Blood	**Type AB** Can have any type of blood Is the universal recipient	**Type O** Can only have O blood Is the universal donor

Antibodies of ABO Blood System

Two types of antibodies are present in blood plasma. The antibodies present together with the antigens in opposite way *i.e.* **Antigen A** with anti-body B, **antigen B** with antibody A, **antigen AB** has no antibodies, none of the antigen with both antibodies A and B. There is an agglutination reaction between similar antigen and antibody. Antigen "A" agglutinates the antibody A and antigen "B" agglutinates the antibody B.

Transfusion Principle

Blood transfusion is the process of transferring blood into one's circulation intravenously. Transfusions are used for various medical conditions such as deficiency of blood, blood lost during pregnancy or any surgery, any blood cell disease like **thalassemia, sickle cell** and **leukaemia**, *etc.*

Before blood transfusion blood group of recipient and donor are tested. If transfusion is carried out between two incompatible blood groups, antigen, antibody reaction will occur in recipient and as a result agglutination *i.e.* clumping of red blood cells will occur. Therefore, the transfusions are carried out on the basis of donor's antigens and recipient's antibodies. Due to these limitations the persons with type A can receive blood from type A or O because they have anti B antibody so they cannot be given any blood carrying B antigen. The person with blood type B can receive blood from a person with blood group B or O. The person with blood group AB can receive blood from all other types *i.e.* A, B, AB and O while a person with blood group O can only receive blood from its own type. Therefore, blood group 'O' is called universal donor and blood group AB is called universal recipient.

Extra Information

An erythroblast is a type of RBC which still retains a cell nucleus. It is intermediate precursor of normal erythrocytes.

Genetic Problem

The woman with blood group B has a child with blood group O what is the genotype of mother and child? What are the genotypes father could have?

Genetic Problem

The father has hybrid blood type 'A' and mother hybrid blood type B what are possible blood groups of their children?

Guess

The blood group O is more frequent in human population. Can you expl-ain why this is so?

Interesting Information

ABO blood group antigens are not only found on the surface of RBCs. They are also normally secreted by some people in their body fluids, including saliva, tears and urine. Such persons are called antigen secretors. Whether someone is able to secrete them is generally controlled by dominant secretor gene "Se" present on chromosome 19.

22.4 Rh Blood Group System and Erythroblastosis Foetalis

Rh blood group system is defined on the basis of Rh factor present on the surface of red blood cells. Rh factor is another blood group system. The ABO blood type is represented by + or – sign. The +ve sign indicates the presence of Rh factor while –ve sign indicates the absence of Rh factor. Landsteiner discovered Rh antigen from the blood of Rhesus monkey in 1930.

Antigens of Rh Blood Group System and Genetic Basis

Rh blood group system is encoded by three genes C, D and E. These genes occupy two loci *i.e.* locus D and C or E loci. Gene D is located on D locus while the gene C or E located on other locus. However, D locus has prime importance. The gene D has two alleles, D and d. D is completely dominant over d. Therefore, the person with DD or Dd are Rh +ve. The person dd genotype is Rh –ve.

The O –ve blood type is **universal donor** because it can donate blood to all blood groups. The AB +ve is **universal recipient** because it can receive blood from all blood groups.

Table 22.4: ABO and Rh Blood Groups system

Recipient	Donor							
	O-	O+	A-	A+	B-	B+	AB-	AB+
O-	✓	✗	✗	✗	✗	✗	✗	✗
O+	✓	✓	✗	✗	✗	✗	✗	✗
A-	✓	✗	✓	✗	✗	✗	✗	✗
A+	✓	✓	✓	✓	✗	✗	✗	✗
B-	✓	✗	✗	✗	✓	✗	✗	✗
B+	✓	✓	✗	✗	✓	✓	✗	✗
AB-	✓	✗	✓	✗	✓	✗	✓	✗
AB+	✓	✓	✓	✓	✓	✓	✓	✓

Extra Information

The positive blood groups can receive all times nega-tive blood groups while negative blood groups can only receive one time positive blood group but not second time.

Anti Rh-antibody and Transfusion Principle

The Rh antibody is not present naturally in the body. This antibody is produced in reaction of Rh antigen. Rh +ve donor is totally incompatible for Rh –ve recipient. Sometimes Rh –ve person receives Rh +ve antigen through wrong Rh +ve blood transfusion. He starts producing anti Rh antibodies against Rh antigen and reaction occurs.

A donor who has never been exposed to Rh antigen can be transfused to Rh +ve recipient.

22.4.1 Erythroblastosis Foetalis

Erythroblastosis foetalis or **hemolytic disease** (Haemo : blood, lytic : breakdown) of new born babies occurs when baby's red blood cells break down at a fast rate. Erythroblastosis foetalis develops in a foetus, when anti-Rh antibodies produced by the mother pass through the placenta and start **hemolysis**.

Problems and Complications in Foetus

Babies who suffer erythroblastosis foetalis, develop the symptoms of anaemia, pale and swollen body at birth. Enlarged liver or spleen. The anaemic foetus starts to release many immature erythroblastosis into his blood system; therefore, the disease is called erythroblastosis foetalis. The anaemic foetus may lead to abortion or still birth. If the pregnancy continues the liver and spleen produce and breakdown RBCs at fast rate. The breakdown of RBCs produces **bilirubin**. The high concentration of bilirubin in foetus blood damages brain and turns the skin yellow. This condition is called **jaundice**.

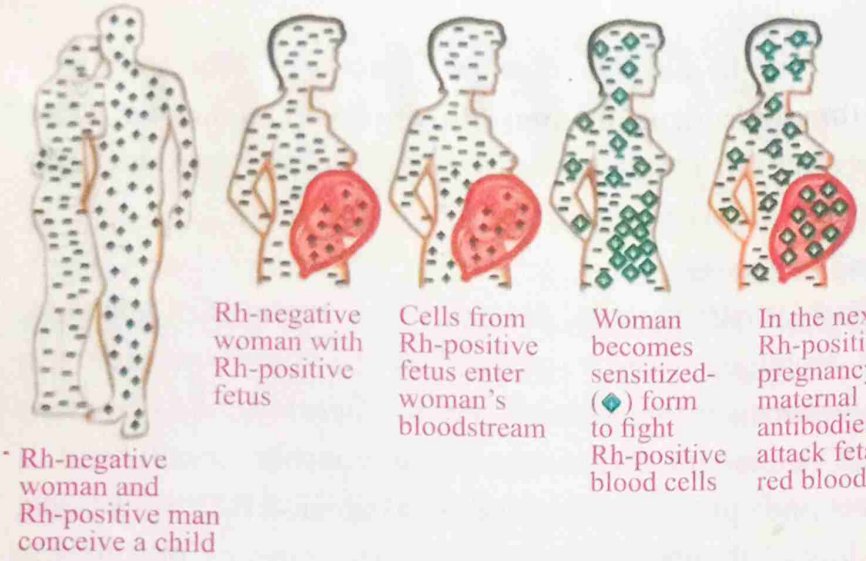
Causes and Risk Factors

The most common cause of erythroblastosis foetalis is **maternal foetal** Rh **incompatibility**. Sometime, an Rh –ve woman marries to an Rh +ve man. The women conceive a child with Rh +ve blood group maternal foetal Rh incompatibility. If the man's genotype is DD, all offspring will have Dd genotype *i.e.* Rh +ve. If the man genotype is Dd, half of the offsprings will be Dd *i.e.* Rh +ve while half of the offsprings will have genotype dd *i.e.* Rh –ve.

The Rh –ve offspring will remain safe in mother body but Rh +ve offsprings will be at risk in mother's body. Can you guess how?

Prevention and Treatments

During a pregnant woman's first prenatal doctor's visit, she should be screened for blood and Rh type. If she has Rh-negative blood, the father's blood and Rh type should be tested. If the father has Rh-positive blood, then Rh-positive foetus may develop in the woman. In this cause the Rh sensitization of Rh-negative mother can be avoided by a simple therapy. In this therapy she is given an injection of Rh antiserum (serum containing anti-Rh antibodies) during early pregnancy (1st trimester) and immediately after birth within 72 hours of delivery. This causes any of the baby's red blood cells that may have crossed into the mother's blood to be destroyed before sensitizing the mother's immune system to produce maternal anti-Rh antibodies. The injected antiserum disappears before the next pregnancy. This has to be done with each pregnancy whether it ends in a delivery or an abortion. (Fig.22.4)



Genetic Problem

An Rh negative woman marries to an Rh positive man. The father of man was also Rh –ve. What will be the possible genotypes of their offsprings? What will be the chances of erythroblastosis foetalis?

Fig.22.4: Maternal Foetal Rh-incompatibility

22.5 Polygenic Inheritance and Epistasis

Polygenic inheritance, also known as **quantitative inheritance**, refers to a single inherited phenotypic trait that is controlled by two or more different genes.

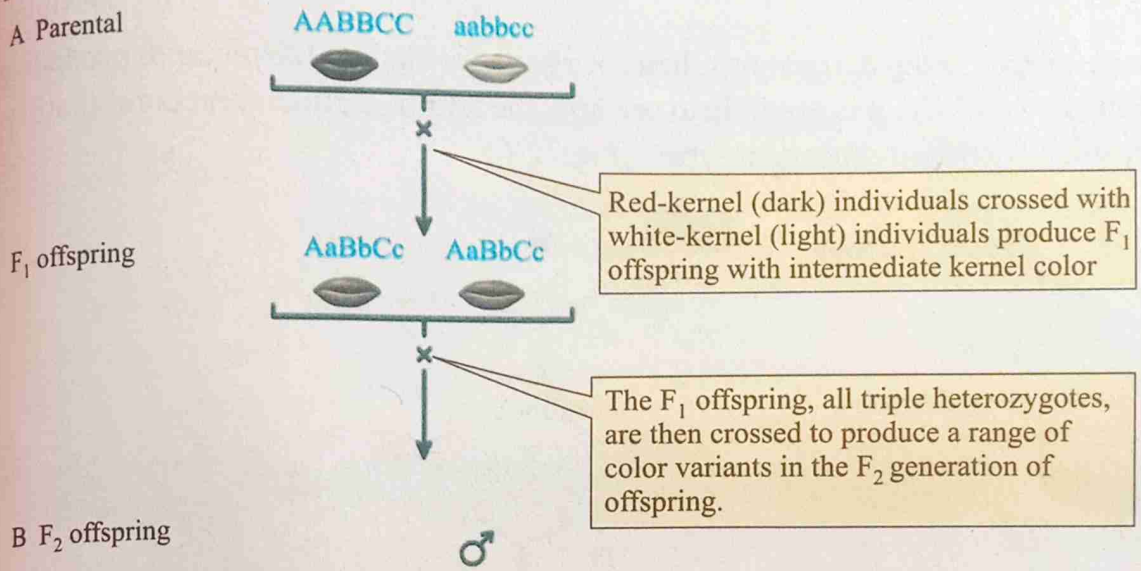
The traits that are determined by polygenic inheritance are not simply an effect of dominance or recessive trait and do not exhibit complete dominance. Infact polygenic inheritance exhibits incomplete dominance so the phenotype displayed in the offsprings, is a mixture of phenotypes displayed by the parents. Each of the genes that contributes to a polygenic trait has an equal influence and each of the alleles has an additive effect on the phenotype outcome.

The polygenic inheritance should not be confused with the effects caused by multiple alleles.

22.5.1 Wheat Grain Colour (an example of polygenic inheritance)

Nilsson Ehle performed many crosses between varieties of wheat having red seeds and those having white seeds. The noteworthy feature of his experiment was the variation in the intensity of the red pigment in the wheat grains produced by F_2 plants. There were many gradations from the deep red of one parent to pure white of the other parent so that plant could be divided into 7 different colour classes in the ratio of 1, 6, 15, 20, 15, 6, 1. Nilsson Ehle could distinguish 6 phenotypic classes with varying intensities of red as follows: 1 deep red, 6 dark red, 15 reds, 20 mediums red, 15 light red and 6 very light red. Only one of 64 plants produced completely white grain and other one of 64 had red grains identical to the parents in the first cross. (Fig.22.5)

Nilsson Ehle postulated three pairs of genes controlling grain colour in wheat with genes for red (ABC) dominant over genes for white abc. It is also appeared that all alleles contributed equally in the production or absence of red pigment. Each of the three gene pairs when considered singly in crosses segregated in expected Mendelian fashion producing F_2 progeny of three red and 1 white.



All contributing	= 1/64
5 contributing	= 6/64
4 contributing	= 15/64
3 contributing	= 20/64
2 contributing	= 15/64
1 contributing	= 6/64
All non-contributing	=1/64

Fig.22.5: Inheritance of Wheat Grain Colour

22.5.2 Inheritance of Human Skin Colour

The pigment melanin is responsible for dark coloration in the skin and there are at least three genes, which control human skin colour. Using a hypothetical example where the production of melanin is controlled by contributing alleles denoted as A, B and C resulting in dark skin colour, and therefore, light skin color is

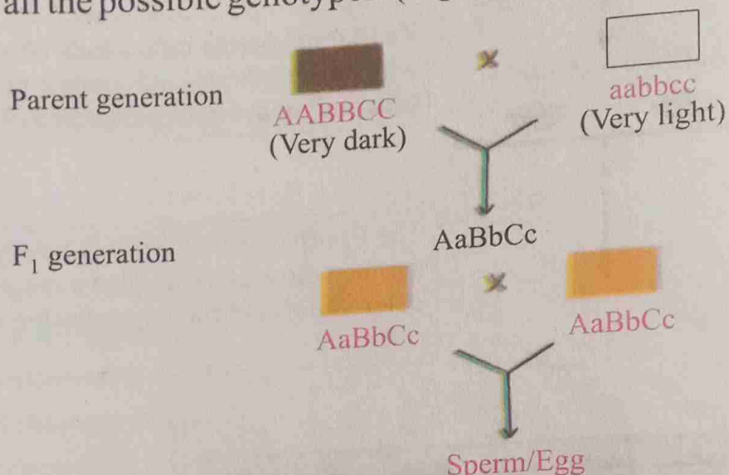
What is Pleiotropy?

The ability of a single gene to have multiple phenotypic effects *e.g.* sickle cell anaemia causes multiple systems, only one of which is the actual sickle celled conditions.

produced by non-contributing allele, denoted as a, b and c, it is possible to see how the spectrum of different skin color can result in the offsprings.

It is important to remember that in polygenic inheritance alleles do not display dominance over other rather each contributing allele gives an additive effect rather than masking effect, and so the way that the alleles interact is different to those in Mendalian genetics.

In an example using two parents, heterozygous for each of the melanin producing genes AaBbCc × AaBbCc, it is possible to see how the additive effects and combinations of alleles result in all the possible genotypes. (Fig.22.6)



Male

Gametes	ABC	ABc	AbC	aBC	Abc	aBc	abC	abc
ABC	6	5	5	4	5	4	4	3
ABc	5	4	4	3	4	3	3	2
AbC	5	4	4	3	4	3	3	2
aBC	4	3	3	2	3	2	2	1
Abc	5	4	4	3	4	3	3	2
aBc	4	3	3	2	3	2	2	1
abC	4	3	3	2	3	2	2	1
abc	3	2	2	1	2	1	1	0

Female

F_2 generation

Very light fair | Very fair | Fair | Light brown | Medium brown | Brown | Very Dark

Fig.22.6: Inheritance of Human Skin Colour

22.5.3 Epistasis

"Epistasis" is a word composed of Greek roots that means "standing upon". The epistasis is a form of interaction between non allelic genes in which one combination of such genes has a dominant effect over other combinations. A gene is said to be **epistatic** when its presence suppresses the expression of a gene which is present on another locus of same or other chromosome.

The gene which is suppressed is known as **hypostatic gene**.

Epistasis is different from dominance because dominance is the phenomenon in which the alleles of the same locus interact with each other to produce a phenotype. While epistasis is a type of interaction that occurs between alleles of different loci. (Table 22.5)

Bombay Phenotype

The Bombay Phenotype discovered in 1952 in Bombay city of India. Individuals with the Bombay phenotype have the genes to make the ABO antigen at one loci but lack the genes that produce the H substance produced at another locus. Individual with Bombay phenotype can receive blood from other individual with blood group O but cannot donate blood.

Table 22.5 Difference between Dominance and Recessive Epistasis

S.No.	Epistasis	Dominance
i)	This type of gene interaction involves two non-allelic pairs of genes.	In this type only one pair of gene is involved, therefore, there is no interaction.
ii)	One pair of gene masks the effect of another pair of genes.	An allele mask the effect of another allele of the same gene pair.
iii)	Expression of both the dominant and recessive alleles may be suppressed by the epistatic gene.	Expression of recessive allele is masked by dominant allele.

Relationship of Epistasis with Polygenic Inheritance

The epistasis is a type of polygenic inheritance where the alleles at one gene locus can hide or prevent the expression of alleles at a second gene locus. **Labrador retrievers** (type of dog) one gene locus affects coat colour by controlling how densely the pigment eumelanin is deposited in the fur. A dominant allele (B) produces the black coat while the recessive allele (b) produces a brown coat color. However, a second gene locus control whether any eumelanin at all is deposited in fur. Dogs that are homozygous recessive at

Continuous and Discontinuos Variation

Continuous variation is where there is complete range of measurements from extreme to another *e.g.* height, weight, skin color. Discontinuous variations are where individuals fall into distinct categories *e.g.* pea plants with either purple flower or white flower, tongue roller and non-roller in human.

this locus (ee) will have yellow fur no matter which alleles are at the first locus.

The polygenic inheritance is not controlled by a single gene locus, but by the combined interaction of many gene loci. In epistasis, the interaction between genes is antagonistic, such that one gene masks or interferes with the expression of another. An example of epistasis is pigmentation in mice. The white type coat color, agouti (AA), is dominant to solid colored fur (aa). However, a separate gene (c) is necessary for pigment production. A mouse with a recessive (c) allele at this locus is unable to produce pigment and is albino regardless of the allele present at locus "A". Therefore, the genotype AAcc, Aacc and aacc all produce the same albino phenotype. A cross between heterozygotes for both genes AaCc × AaCc would generate offspring with a phenotypic ratio of an agouti 3 solid color: 4 albinos. In this case, the gene 'c' is epistatic to the 'A' gene.

Coat Color in Labrador Retriever

The Labrador retriever is highly popular type of dog found all over the world. This dog is trained to perform different task *e.g.* screening and detection work for law enforcement agencies. These are also used for hunting. There are three basic coat color in the Labrador: black, yellow and chocolate. (Fig.22.7)

Fig. 22.7: Three types of Labrador Retriever

In Labradors, the B and E genes result in black, yellow and chocolate Labrador *e.g.* BB become a black Labrador. The Bb dog is also black but it carries the chocolate gene which can be passed on its offspring. So bb genotype have chocolate Brown coat color while yellow Labrador is characterized by a recessive epistatic gene (ee). But every Labrador retriever has both sets of genes which can come in any combination of capital and lower case letters *i.e.* dominant and recessive alleles. Regardless of the combination of B genes, any time the ee genotype is present, it masks the B coloration *e.g.* BbEE dog would have a black coat but Bbee dog would have a yellow coat. The black Labradors are dominant, therefore, having the most possibilities. Both yellow and chocolate Labradors are recessive, but because a yellow Labradors 'ee' genes mask both the black and chocolate coloration. So yellow Labradors are more common than chocolate Labrador. (Fig.22.8)

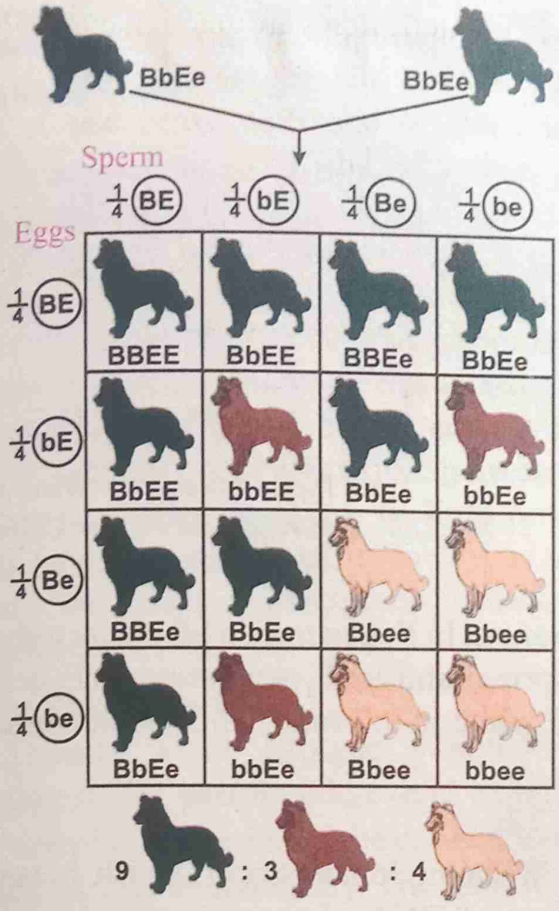


Fig.22.8: Inheritance of Coat Color of Labrador Retriever

Genetic Problem

Based on the combination of alleles can you determine what coat color a Labrador puppy could have if its father was BbEE and its mother bbEe?

Genetic Problem

When two chocolate colored Labradors were crossed, a yellow puppy was born, what is the possibility of yellow coat colored puppy if the parents are again crossed?

Inheritance of Flower Color (Pigment phenotype) of Sweet Pea *(Lathyrus odoratus)*

Batson and Punnett studied the genetic control of flower color in the sweet pea. It is an example of duplicate recessive epistasis. The flowers in this plant are either purple or white. The flowers will be purple if they contain anthocyanin pigment and flowers will be white if they do not contain this pigment. The production of anthocyanin is controlled by two different gene loci. The presence of at least single dominant allele of both the gene pairs is required for the production of anthocyanin. The dominant allele of one gene 'A' acts on a colorless precursor (substrate A) to produce an intermediate colorless product, which on getting activated by dominant allele of the second gene 'B' result is the formation of anthocyanin pigment leading to production of purple colored flower. Thus dominant alleles 'A' and 'B' complement each other to produce purple color. This type of interaction is also called

Mutation

Mutation is a change in either the amount or arrangement of genetic material (DNA). If a mutation occurs in gamete, the resulting genetic change can be inherited. There are also mutations which occur in normal body cells. These are called somatic mutations. They are responsible for different type of cancer and not transmitted in offsprings.

complementary gene interaction because it involves the interaction of both the genes. If anyone locus has homozygous recessive genotype *i.e.* AAbb or aaBB then it will interfere with dominant allele and hide their expression of purple color and flowers will be white in color. In this case the epistatic alleles are recessive and both types of recessive alleles cause same epistatic effect so this type of epistasis is called duplicate recessive epistasis.

Parents: Purple flower AABB × White flower aabb

F_1: AaBa Purple flower

	AB	Ab	aB	ab
AB	AABB [P]	AABb [P]	AaBb [P]	AaBb [P]
Ab	AABb [P]	Aabb [W]	AaBb [P]	Aabb [W]
aB	AaBb [P]	AaBb [P]	aaBB [W]	aaBb [W]
ab	AaBb [P]	Aabb [W]	aaBb [W]	aabb [W]

P = Purple flower, W = White flower

Fig.22.9: Inheritance of Flower Color in Sweet Pea

Batson and Punnett crossed white flower plant AAbb with another white flowered plant aaBB and got F_1 generation. In F_1 generation all plants were purple flower plants. Then they self-crossed F_1 offsprings and got F_2 generation. In F_2 generation they got two types of plants *i.e.* purple and white in 9:7 ratio. This result confirms the duplicate recessive epistasis. (Fig.22.9)

22.6 Gene Linkage and Crossing Over

The term gene was introduced by Wilhelm Johannsson (Danish botanist and geneticist) in 1909. Gene is a small segment of DNA as chromosome. It consists of specific sequence of nucleotides which code a specific protein or polypeptide chain. The place on chromosome where the gene resides is called the **gene locus**. Mendel did not know about gene. He used the term **factor or element** which is now called gene.

22.6.1 Gene Linkage

Genes that are located on the same chromosome are called linked genes. Alleles for these genes tend to segregate together during meiosis, unless they are separated by crossing over. Crossing over occurs when two homologous chromosomes exchange segments during meiosis. The close together two genes are on a chromosome, the less likely their alleles will be separated by crossing-over.

Linkage explains why certain characteristics are frequently inherited together *e.g.* genes for hair color and eye color are linked, so certain hair and eye colors tend to be inherited together such as brown hair with blue eye.

If genes are linked at autosomes, called **autosomal linkage** and if genes are linked on sex chromosomes, called **sex linkage**. Linked genes violate the law of independent assortment because these genes are not free to participate in independent assortment.

Detection of Gene Linkage

A test cross is an ideal method to know whether the genes are linked or not. Any

deviation from the ratio of offsprings as expected by the law of independent assortment is to be verified for linkage. A test cross with one of the parents being homozygous recessive. All the offsprings exhibit the possible combination of traits in equal ratio if the alleles are not linked and other parents of the original cross is heterozygous. Any significant deviation from this indicates the possibility of linkage. Approaches to test cross can include two-point test crosses for double heterozygous and three point test crosses for analysis with three genes. If offsprings in test cross are all parental types than it is called **complete or light linkage** and if less recombinant and more parental types are produced, then this is called **incomplete or partial linkage.** To determine the effect of linkage on inheritance, Morgan performed an experiment on Drosophila (fruit fly).

SRY Gene Located on Y chromosome encodes a transcription factor protein which controls expression of other genes. It stimulates male development *i.e.* developing testes, secrete anti mullerian hormone and destroy female structure. Testosterone hormone develop the male structure.

Morgan Experiment

Thomas Hunt Morgan (1866-1945) was an American geneticist and embryologist. He performed several experiments on ***Drosophila melanogaster*** (fruit fly). In one of his experiments he crossed long winged and broad abdomen with vestigial wing and narrow abdomen fly. The long wing and broad abdomen are dominant while

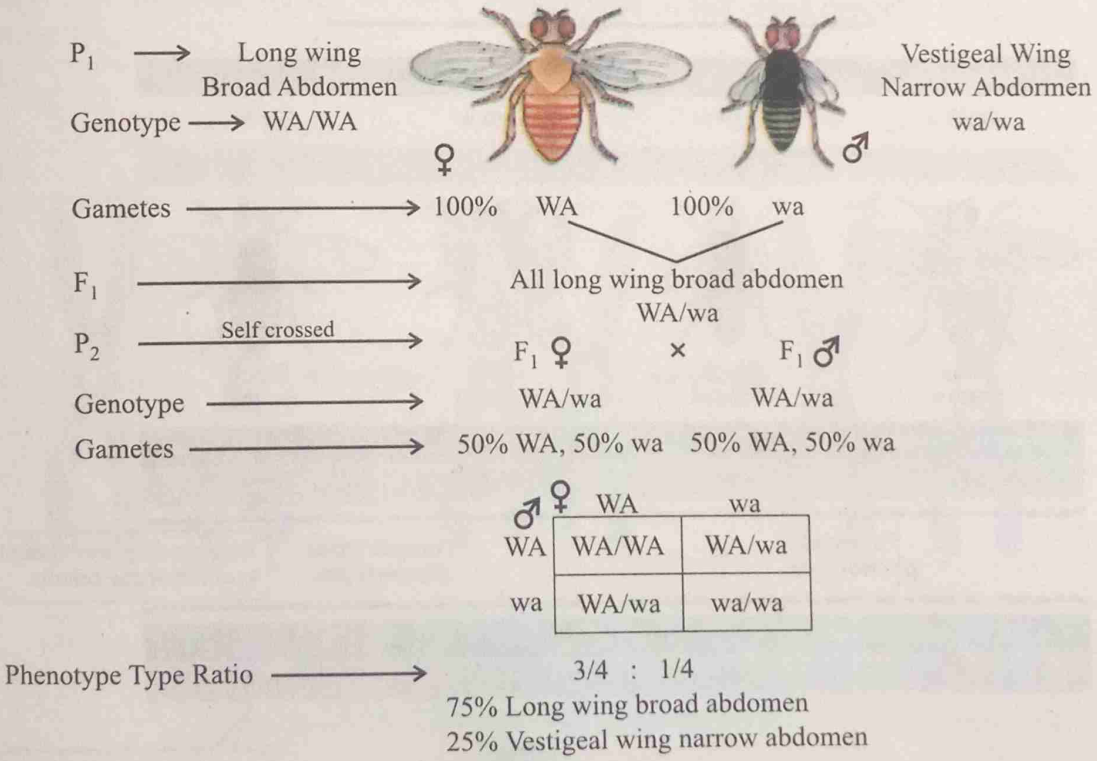


Fig.22.10: Morgan Experiment

vestigial wing and narrow abdomen are recessive traits. So in F_1 generation all flies were long winged and broad abdomen. Then he self-crossed two flies of F_1 generation. In F_2 generation he obtained 3/4 of offspring with long wings and broad abdomen and remaining 1/4 of the total had vestigial wings and narrow abdomen. (Fig.22.10)

Interpretation of Results

These results were unexpected and violation of Mendel's law of independent assortment *i.e.* 9:3:3:1. Morgan concluded that the genes of long wings and broad abdomen located on the same chromosome, so they could not assort independently during meiosis and rather inherited together. Therefore, no recombinant types were produced.

Linkage Detection

Gene linkage can only be detected accurately if the number of offsprings are quite large. It is because the probability *i.e.* chance of occurring an event determine the kind of gametes and chances of their fusion. Thus as large number of offsprings will be, the more chance of accuracy in detection of result. More parental type and less or no recombinant

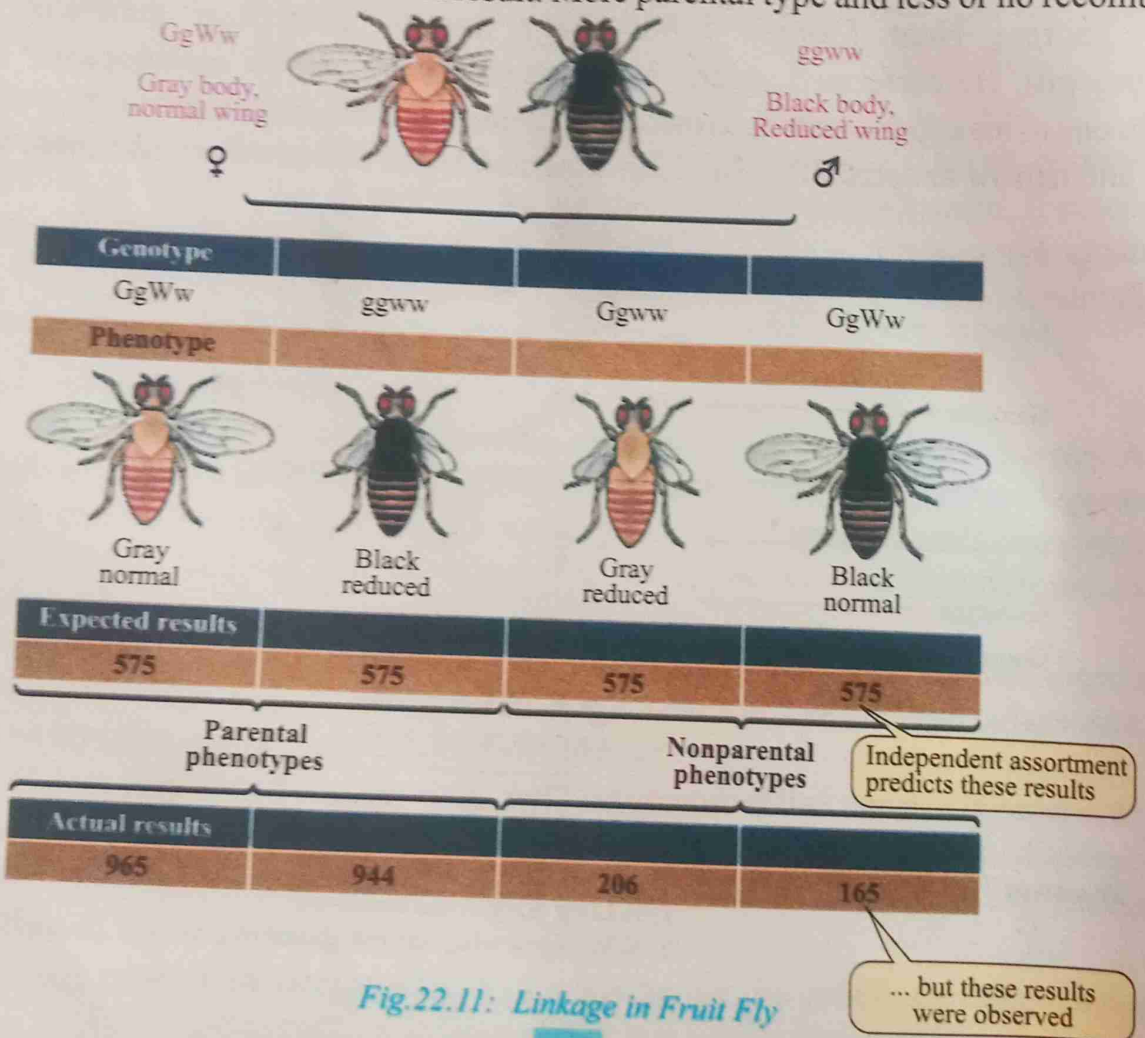


Fig.22.11: Linkage in Fruit Fly

is indication of gene linkage. For detection of linkage Morgan mated the dihybrid (Gg Ww) with recessive parental type flies (gg ww). Morgan's result was very different from the results, he expected based on the law of independent assortment *i.e.* 1: 1: 1: 1, while the actual result were quite different *i.e.* more parental types and less recombinant types. (Fig.22.11)

Crossing Over

During the formation of gametes, the homologous pairs of chromosomes exchange their segments. This process is called crossing over. Crossing over results in a shifting of genetic material and an important cause of genetic variation. The crossing over brings alleles together in new combinations. When these alleles distribute in gametes, a wide variety of gametes are produced. This is why the siblings are not identical. The cross-over data may also be used to determine the location of gene on chromosome *i.e.* gene mapping. (Table 22.6) (Fig.22.12)

Table 22.6: Difference between Crossing Over and Linkage

S. No.	Crossing Over	Linkage
i)	It leads to separation of linked gene.	It keeps the genes together.
ii)	It involves non-sister chromatids of homologous chromosomes.	It involves individual chromosome.
iii)	It increases variability.	It reduces variability.
iv)	It provides equal frequency of parental and recombinant type in test cross progeny.	It provides higher frequency of parental type in test cross progeny.

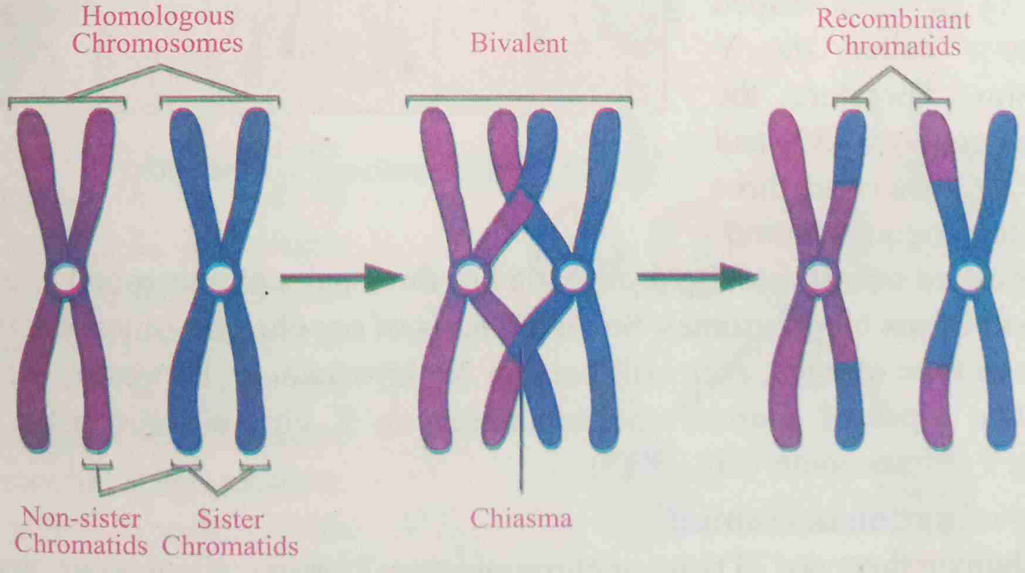


Fig.22.12: Chromosomal Crossing Over

22.8 Sex Linkage

The sex chromosomes (X and Y) contain genes which are related to sexual character (traits) of male and female. However, besides controlling sexual traits, the sex chromosomes also contain other genes which are not concerned with sexual traits. This phenomenon is called sex linkage *e.g.* gene for **blood clotting factor VIII**, gene for **opsin pigment** in eye, gene for **hairy pinna**, *etc.* An allele that is located only on X-chromosome (*i.e.* non-homologous portion) is called **x-linked**. The allele that is only located on the (non-homologous portion) of Y chromosome is called **Y-linked or holandric traits**. All those such allele which are located on homologous portion of X and Y chromosome are called **XY linked genes or pseudo-autosomal genes** because their pattern of inheritance is like autosomal genes.

22.8.1 Sex Linkage in Drosophila

T.H Morgan (1910) for the first time discovered sex linkage in Drosophila. Morgan when experimenting noted the sudden appearance of one white eyed male in the culture of normal red eyed Drosophila. This white eyed male was crossed with red eyed female. The F_1 flies were all red eyed indicating that white eye color is recessive to normal red eye color. When these F_1 flies were self-crossed freely, the red and white eyed flies appeared in the ratio 3:1 in F_2 generation. The white eyed flies were male. Among the red eyed flies two third were female and one third

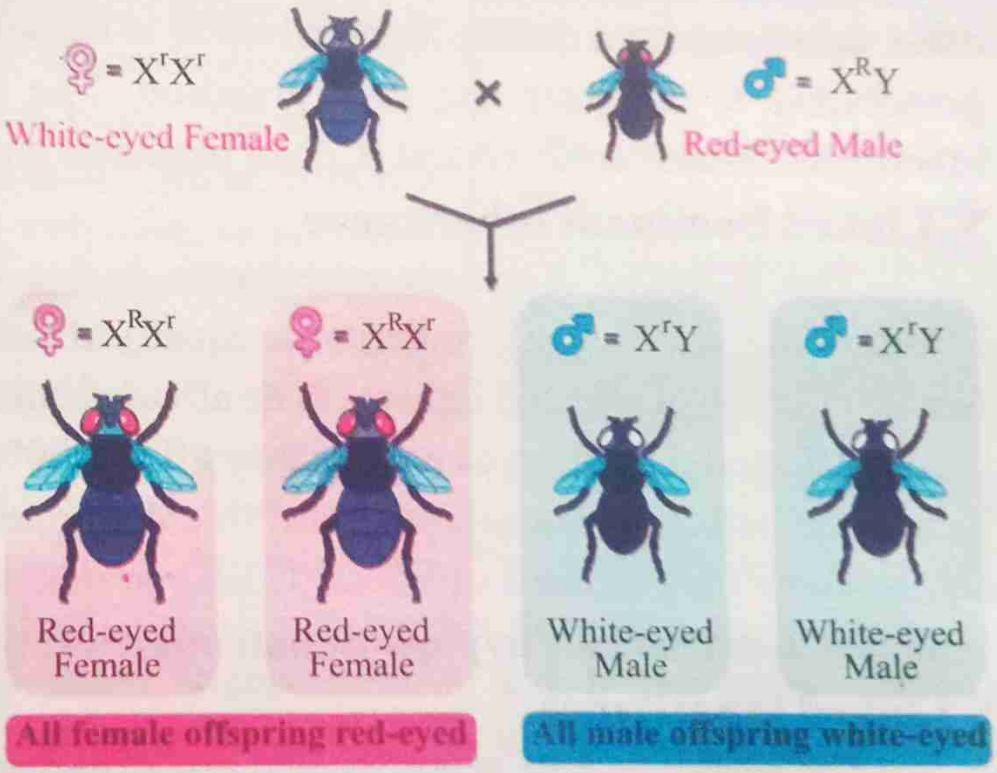


Fig.22.18: Sex determination in Drosophila

were male. The female are all red eyed whereas 50% males were white eyed and remaining 50% male were red eyed. When a reciprocal cross was performed between white eyed female and red eyed male, all female in F_1 generation are red eyed and all male are white eyed. When these two types of individuals from F_1 generation were self-crossed, female population in F_2 generation will consist of 50% red eyed and 50% white eyed individuals.

Similarly, the male population in this generation consists of 50% red eyed and 50% white eyed individual. (Fig.22.18)

Morgan Conclusion

On the basis of these results Morgan concluded that the white eye trait gene is located on X chromosome and this gene is recessive for eye color.

22.8.2 Sex Linkage in Humans

There are many traits in human which are linked with sex chromosomes. The sex linked traits may be X-linked or Y-linked. The X-linked may be recessive or dominant.

X-Linked Recessive Inheritance

The X-linked recessive inheritance is due to recessive allele on X chromosome. These are more common in male than female. It is because female possessing one X-linked recessive is considered carrier. A female for X-linked recessive trait can only be affected if it carries allele on its both X chromosomes. On the other hand, as male has only one X chromosome, so if a recessive allele is present on X chromosome it will express itself. A father cannot donate X-linked allele to his son. So pattern of inheritance is from grandfather to daughter and then grandson. The examples of X-slinked recessive inheritance is haemophilia A and B, color blindness and testicular feminization.

X-Linked Dominant Inheritance

The X-linked dominant inheritance is due to dominant allele present on X chromosome, so this type of inheritance equally affects in male and female. However, all female children of affected father will be affected but no male children of affected father will be affected. The affected mother may affect 100% children if this dominant allele is located on both X chromosomes but if this dominant allele is located only on one sex chromosome then chances of affected children will be 50%. The examples of X-linked dominant inheritance are **hypophosphatemia** (rickets), **incontinentia pigmenti**, *etc.*

Y-Linked Inheritance

The inheritance of genes located on 'Y' chromosome. Since only male have 'Y' chromosome. Therefore some 'Y' linked genes can only be transmitted from father to son. The Y-linked inheritance is also called **holandric inheritance**. The concepts of dominant

and recessive do not apply to Y-linked traits, as only one allele is ever present in any one (male) individual. 'Y' linked inheritance never occur in females. The examples of Y-linked trait in male are **hypertrichosis** (growth of hair on ear pinna), **porcupine man** (straight hair on body) and **webbing of toes**, *etc.* (Fig.22.19)

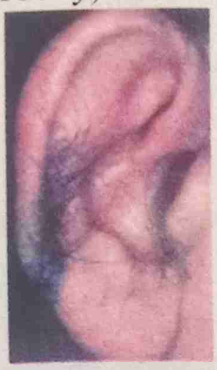


Fig.22.19: Hairy Pinna (Example of Y-linked Inheritance)

Extra Information

Recently two more genes located on Y chromosomes have been discovered.

i) Testis determining factor (TDF).

ii) Minor Histocompatibility gene (H-Y)

22.8.3 Sex Linked Disorders in Human

Sex linked disease are passed down in families through one of the X or Y chromosomes. Some sex linked disorders will be discussed here:

Genetics of Haemophilia

It is a serious disease of human in which blood fails to clot after it starts flowing from an injury site of haemophilia patient. It is an X-linked recessive trait *i.e.* its recessive allele is located on 'X' chromosome, say X^h. Its dominant allele says X^H favors blood clotting. It is very rare in females as female requires allele from her both father and mother which is very rare, as very few diseased males survive to marry and reproduce. On the other hand, male can easily get this disease, as they only need to get a recessive gene form the mother.

History of Haemophilia

The haemophilia is called royal disease because haemophilia gene was passed from Queen Victoria, who became Queen of England in 1837 to ruling families of Russia, Spain and Germany. Queen Victoria's gene of haemophilia was caused by spontaneous mutation.

There are three types of haemophilia *i.e.* haemophilia A, B and C. The allele for haemophilia A and B are located on X chromosome, so these two types are X linked. The allele for haemophilia C is located on autosome, so its chances are equal in male and female. However, haemophilia A and B are more common. Haemophilia A is caused due to missing blood clotting factor VIII and is about 80% of total haemophiliac patients. Haemophilia B is due to absence of blood clotting factor IX and it is about 20%. haemophilia C is due to missing of blood clotting factor XI and it is very rare (less than 1%).

Table 22.7: Comparison between different Types of Haemophilia

A	B	C
It is most common type.	It is 2nd most common type.	It is least common.
It is very severe.	It is moderate.	It is mild.
It is caused by missing of blood clotting factor VIII.	It is caused by blood clotting factor IX.	It is caused by blood clotting factor XI.

Genetics of Color Blindness

Color blindness is not a form of blindness at all, but a difficulty in distinguishing certain colors, such as blue, yellow, red and green. The color blindness is infact a color vision deficiency. It is X-linked recessive inheritance, therefore, more common in males than females. There are three fundamental colors. *i.e.* Red, green and blue. There are two types of photoreceptor cells in retina of eye *i.e.* Rod and cone cells. The rod cells are more abundant but these are incapable of perceiving color. The cone cells are responsible for color vision. There are three types of cone cells *i.e.* red, green and blue color receiving. The cone cells can receive these colors if they have opsin proteins. The three type of opsin protein is coded by different genes. The gene for red and green opsin are on X chromosomes while gene for blue opsin is on chromosome No.7 which is autosomal chromosome, so equally expressed in male and female. The color blindness may be in the form of dichromacy and monochromacy.

Extra Information

Some women can have a genetic mutation that makes them **tetra chromatic**, which causes their eyes to have 4 different types of cone cells enabling them to see 1000 million different colors as compared to a normal person who can see 100 million.

Dichromacy

A color blind patient with dichromacy can perceive two primary colors but unable to one primary color so dichromacy can further have three sub types

1) **Protanopia** is red color blindness.
2) **Deuteronopia** is green color blindness.
3) **Tritanopia** is blue color blindness.

Monochromacy

It is severe type of color blindness in which patient perceive only one color. It is true color blindness. Usually monochromate cannot perceive red and green colors. It's pattern of inheritance is same as other X-linked recessive inheritance like haemophilia. (Fig.22.20)